REMARKS

Reconsideration and withdrawal of the rejections of the application are requested in view of the amendments and remarks presented herein, which place the application into condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 2, 4-9, 12-21, 28, 34, 35 and 38 are under consideration. Claim 2 is amended to clarify the definition of "CDR loop structure." Support for the amendment can be found on page 3, lines 8-10, page 5, lines 28-29 and page 13, line 12, of the specification. No new matter is added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art, and that these claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that these amendments should not give rise to any estoppel, as they are not narrowing amendments.

II. THE ART REJECTIONS UNDER 35 U.S.C. §§ 102 AND 103 ARE OVERCOME

Claims 2, 7-9, 12, 13, 20, 21, 28, 34, 35 and 38 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Peach *et al.* Claims 2, 13 and 14 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peach *et al.* in view of Bogden *et al.* Claims 2 and 15-17 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peach *et al.* in view of Cai *et al.* Claims 2, 4-6, 18 and 19 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Peach *et al.* in view of Koide. The rejections are traversed, and will be addressed collectively.

According to the Advisory Action, it would appear as though the Examiner has construed the definition of "CDR loop structure" as encompassing (1) a surface polypeptide loop structure OR (2) a surface polypeptide loop region like the complementarity determining regions in antibody V-domains. Under the broader definition of (2), "CDR loop structure" could

potentially be read as encompassing an entire V-like domain. This is not the intended scope of the claims.

As has been explained previously, and as the specification, taken as a whole, clearly teaches, CDR loop structures are within V-like domains. (See page 4, lines 18-19.) The language of claim 2 has been modified, consistent with the specification, to clarify the definition of "CDR loop structure" and highlight this point. From the claim language, it is clear that a CDR loop structure is only a portion of the V-like domain (*i.e.* corresponding to a complemenatarity determining region that is part of the antibody V-domain), and is not equivalent to the entire V-like domain.

In addition, the Advisory Action makes reference to the homologue mutant HS2 disclosed in Peach *et al.*, stating:

> [T]he region where the CTLA-4-derived sequence is longer than the CD28-derived sequence by one amino acid in the HS2 construct (Figures 3 of Peach *et al.*) appears to be located on the surface of the HS2 molecule (compare the alignment in Figure 1 with the model in Figure 6 of Peach), and as such is located within a "surface polypeptide loop structure" as required by the definition on page 5 of the instant specification.

The HS2 mutant is a CTLA-4 derived V-domain in which the sequence between residues 21 and 94 has been substituted by the corresponding CD28 sequence. Based on the sequence alignments of CTLA-28 and CD28 presented in Figure 1 of Peach *et al.*, CTLA-4 has one additional residue (threonine) at position 45 and CD28 has two additional residues (glutamate or glycine and phenylalanine) at positions 65 and 66, respectively. Therefore, between positions 21 and 94, CD28 has one additional amino acid residue as compared with CTLA-4. However, the Advisory Action refers to the CTLA-4-derived sequence as being longer than the CD28-derived sequence, which is clearly not the case.

It is true that the HS2 mutant, as a result of the wholesale CD28 substitution, is longer by one amino acid between residue positions 21 and 94. However, the Advisory Action then appears to contend that Figure 6 somehow indicates that the residues at positions 65 and 66 of the CD28 insert are on the surface of the HS2 molecule. It is unclear how this conclusion was reached. Irrespective of whether the residues at positions 65 and 66 of the CD28 insert are on the surface or not, these residues are nowhere near a CDR loop structure corresponding to a CDR of an antibody V-domain, as is evidenced by Figure 1 of Peach *et al.*

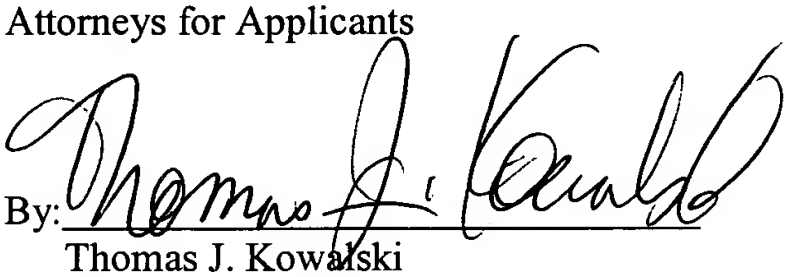
The language added to claim 2 clarifies the definition of "CDR loop structure," and the arguments herein and previously filed demonstrate that Peach *et al.* does not teach or suggest the claimed invention. Moreover, the combination of Peach *et al.* with any or all of the cited secondary references would still not lead the skilled artisan to the claimed invention. Accordingly, reconsideration and withdrawal of the art rejections are requested.

CONCLUSION

This application is in condition for allowance. In an effort to end the delays and inefficiencies that have predominated in the prosecution of this application, Applicants' representative will contact the Examiner and his SPE to arrange a personal interview and expedite the resolution of any remaining issues. Should the Examiner wish to allow the application as a result of the amendments and arguments presented herein, said interview will not be necessary. Applicants look forward to receiving a Notice of Allowance.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: 

Thomas J. Kowalski
Reg. No. 32,147

Anne-Marie C. Yvon, Ph.D.
Reg. No. 52,390
(212) 588-0800